REMARKS

Claims 50, 52-56, 58, 59, and 61 are pending in this application.

Claims 50, 52, 55, 56, 58, and 59 have been amended.

Claims 1-49 and 62-65 have been cancelled without prejudice as being directed to non-elected subject matter.

Claims 51, 57 and 60 have been cancelled as being redundant in view of the amendments to claims 50, 55, and 58.

Claims 50 and 55 were objected to for depending from non-elected claims. In response, claims 50 and 55 have been amended to place the claims in independent form. Amended claims 50 and 55 both incorporate the limitations of claims 1 and 51. In addition, claim 55 has been amended to replace the term "patient" with "mammal" to be consistent with dependent claim 56.

Claim 52 has been amended to change its dependency from cancelled claim 51 to claim 50.

Claims 56 and 59 have been amended to include the additional step of transfecting the cells with a gene encoding an antiangiogenic peptide.

Claim 58 has been amended to specify that the stem cell population is transfected with a gene that encodes an antiangiogenic peptide and to replace the term "patient" with the term "mammal."

Support for these amendments can be found in the original claims and in the specification on page 3, lines 1-5, page 8, lines 13-16, page 9, lines 15-20, and on page 24, line 17 through page 25 line24. No new matter is added by these amendments.

The Claimed Methods Meet the Enablement Requirement of §112.

Method claims 55, 56, 58, 59, and 61 stand rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the enablement requirement. This rejection is in error and should be withdrawn. The gist of the rejection appears to be that the specification does not provide enough data to apprise one of ordinary skill in the art how to *make and use* the invention, with particular emphasis on *how to use*. The Office Action clearly applies the wrong standard for utility to the present method claims. The how-to-use

prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. §101 that the specification disclose as a matter of fact a practical utility for the invention. *In re Kirk*, 376 F.2d 936, 942, 153 USPQ 48, 53 (CCPA 1967). The threshold of utility is not high. An invention is "useful" under §101 if it is capable of providing *some* benefit. *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999), emphasis added.

In addition, the Office Action seems to equate the presently claimed methods with methods of treating or, more specifically methods of "curing" a disease. That characterization is incorrect. Claims 55 and 56 are directed to methods of inhibiting angiogenesis in the eye. Similarly, claims 58, 59, and 61 are directed to methods of delivering a gene encoding an antiangiogenic peptide to the eye. These claims are not directed to treatment of a disease *per se*. In order to clarify this point, claims 55, 58, have been amended to replace the term "patient" with the term "mammal", which also makes these claims consistent with their respective dependent claims 56 and 59, both of which recite the step of isolating bone marrow cells from a mammal. Inhibition of angiogenesis is a *tool*, which can be used therapeutically or can be used as a research tool to induce vascular changes in the eye of a mammal (e.g., to model a vascular disease or to provide a screening tool for vascular promoters, and the like). Either use represents sufficient utility to satisfy the how-to-use prong of §112 (i.e., "some benefit"). *See Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, cited above.

As noted above, the present claims are directed to methods of inhibiting angiogenesis in the eye and to methods of delivering a gene encoding an antiangiogenic peptide to the eye. Both of these effects are clearly demonstrated, in animal models, by the working examples and data presented in the application. In addition, the specification clearly teaches how to make the isolate the stem cells, how to transfect them, and how to administer them to the eye. Accordingly, the application does teach one of ordinary skill in the art how to make and use the invention.

Even if, *arguendo*, the claims are characterized as therapeutic methods for treating an ocular disease, such treatment can be useful despite some potential adverse side affects in some patients. An ocular treatment may be useful for some subjects even where only partial improvement in visual sensation is restored or where further degradation in vision

is only slowed. There is no requirement in the law or in medicine that a treatment must "cure" a disease or be without some risk. Even great risk may be acceptable in some situations (e.g., where a patient is suffering from a terminal illness). Furthermore, utility does not impose a requirement of commercial marketability. See *Studiengesellschaft Kohle v. Eastman Kodak Co.* 616 F.2d 1315, 1339, 206 USPQ 577, 598 (5th Cir. 1980).

The Office Action points to the articles by Smith and by McFarland *et al.*, both of which were published *after the effective filing date of the present application*, as evidence of uncertainty in the art at the time the invention was made. McFarland *et al.* is inapt because it does not even address the use of *transfected stems cells* as a vector for delivery of transgenes, its late publication date notwithstanding. While Smith does comment on some of the data that was included in the present application, even the portions of the Smith article cited on page 5 of Office Action, reflect *positively* on the use of the novel stem cells disclosed by Otani *et al.* to deliver therapeutic drugs to the eye (e.g., "The use of stem cells as drug delivery vehicles has great potential. . . "), clearly supporting the patentability of the present claims.

For the foregoing reasons, the rejection of claim 55, 56, 58, 59, and 61 for lack of enablement should be withdrawn.

Claims 55, 56, 58 and 59 Are Not Indefinite.

Claims 55, 56, 58 and 59 stand rejected as being indefinite beacuse original claim 55 depended from claim 49, which did not provide antecedent basis for the reference to a "transfected stem cell population". The dependency of claim 55 on claim 49 was clearly a typographical error. The above-described amendment to claim 55 renders this ground for rejection moot, since claim 55 is now in independent form and directly specifies the characteristics of the stem cell population.

Claim 50 is not anticipated by Wilson *et al.*

Claim 50 stands rejected as being anticipated by Wilson *et al.* This rejection is unwarranted. Claim 50 has been amended to incorporate the limitations of claim 51, which was not included in the rejection. Claim 50 is directed to a transfected stem cell population in

which at least 50 % of the cells include the CD31 and c-kit cell surface antigens and which is transfected with a gene encoding an antiangiogenic peptide. The stems cells have a surprising affinity for activated astrocytes within the retina of the eye. When the cells are injected into the interior of the eye, the cells specifically home in on astrocytes, which are cells that provide a structural and functional interface between the vascular network and the neurons, i.e., forming a template for the retinal vasculature (*see* the specification at page 17, line 10 through page 18, line 16).

Wilson *et al.* does not teach or even suggest the presently claimed transfected stem cell population. In particular, the reference does not teach or suggest a stem cell population transfected with a gene encoding an antiangiogenic peptide, as acknowledged on page 11 of the Office Action. Wilson *et al.* merely speculate about using the stems cells for gene therapy. Accordingly, this ground for rejection should be withdrawn.

Claims 52-54 are Not Obvious in View of the Applied Art.

Claims 52-54 also stand rejected as being obvious over Wilson *et al.* in view of Schimmel *et al.* This rejection is unwarranted, as well. As noted above, Wilson *et al.* do not teach or suggest transfecting stem cells with a antiangiogenic peptide, and certainly not an antiangiogenic fragment of TrpRS, such as T2-TrpRS, as required by claims 53 and 54. There is no working example in the reference of a successfully transfected stem cell. At best, Wilson *et al.* provide an invitation to experiment, nothing more. The Schimmel *et al.* reference does not cure this defect.

Schimmel *et al.* disclose that the T2 fragment of TrpRS is a potent antiangiogenic peptide. Schimmel *et al.* also disclose transfecting a cell line *for purposes of propagating therapeutic viral vectors.* Schimmel *et al.* do not teach or suggest transfecting stem cells with a gene encoding T2-TrpRS. The only therapeutic vectors discussed by Schimmel *et al.* are viral vectors.

One of ordinary skill in the art would not have had a reasonable expectation of success in combining the teachings of Wilson *et al.* and Schimmel *et al.* to arrive at the presently claimed stem cell lines. Schimmel *et al.* deals with viral vectors, while Wilson *et al.* merely speculates about transfecting the purportedly novel stem cells disclosed in the

reference. There is certainly no teaching or suggestion in the combined references of the unexpected advantage that a transfected stem cell population in which at least about 50% of the cells include the CD31 and c-kit cell markers can selectively target astrocytes within the retina, as do the stem cells of the present claims. This rejection appears to be founded on an "obvious to try" standard, which is not the standard of §103. *See In re Geiger*, 815 F.2d 686, 2 USPQ 2d, 1276 (Fed. Cir. 1987). A *prima facie* case for obviousness requires that the references both suggest the claimed subject matter and reveal a reasonable expectation of success to one skilled in the art. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1988). There is nothing in the references themselves that would have provided a reasonable expectation of producing transfected stem cells having the unexpected astrocyte targeting properties of the claimed stem cells. This is particularly so in view of the Examiner's contention that the art is unpredictable. Absent such a teaching, the present rejection cannot stand.

Conclusion.

Applicants deem all of the present claims to be supported by an enabling disclosure and to be patentable over the applied art. Reconsideration and early allowance of all pending claims is solicited.

Respectfully submitted,

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